Diabetes Mellitus: A Comprehensive Clinical Masterclass

An **evidence-based** overview of pathophysiology, diagnosis, and management.

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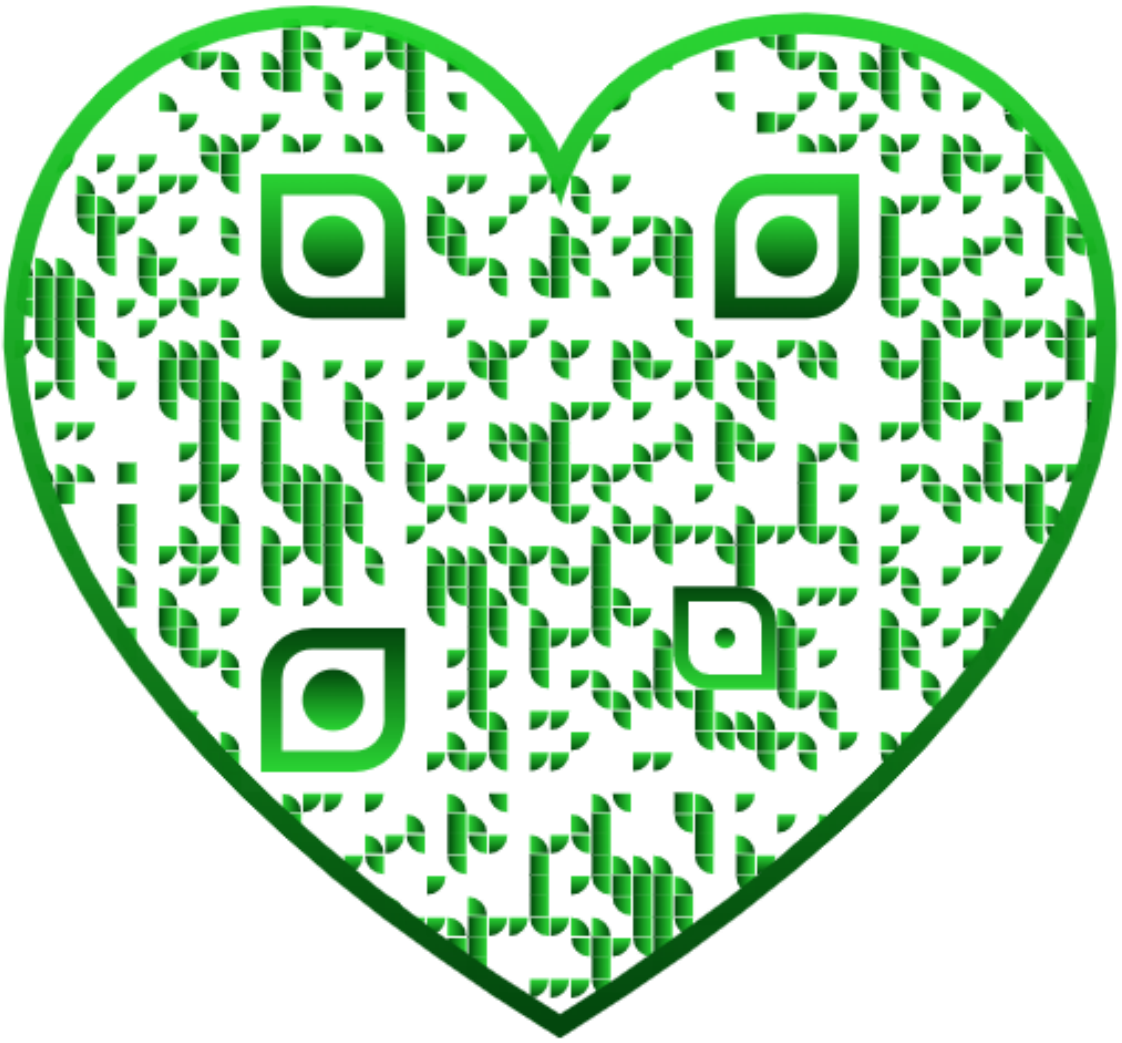
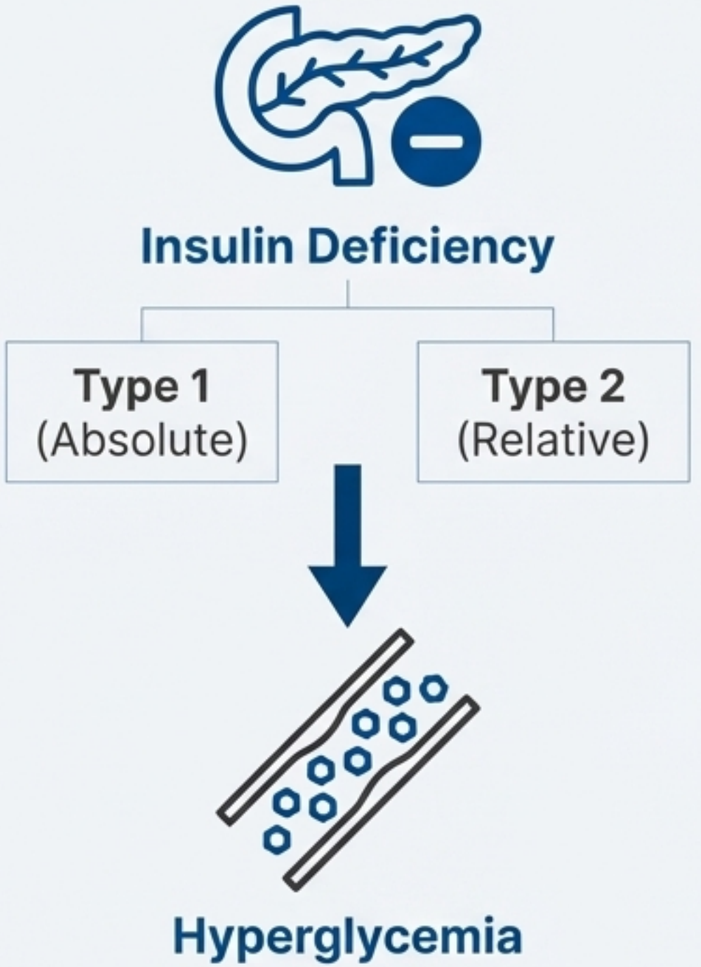


Defining Diabetes Mellitus

Diabetes Mellitus is a clinical metabolic syndrome characterized by hyperglycemia. This elevated blood glucose level results from a deficiency of insulin, which can be:

- **Absolute:** A complete lack of insulin production, characteristic of **Type 1** diabetes.
- **Relative:** The body's inability to effectively use the insulin it produces (insulin resistance) or an insufficient amount of insulin for the body's needs, characteristic of **Type 2** diabetes.

This chronic hyperglycemia leads to a cascade of clinical symptoms and long-term anatomical, histological, and pathological changes.



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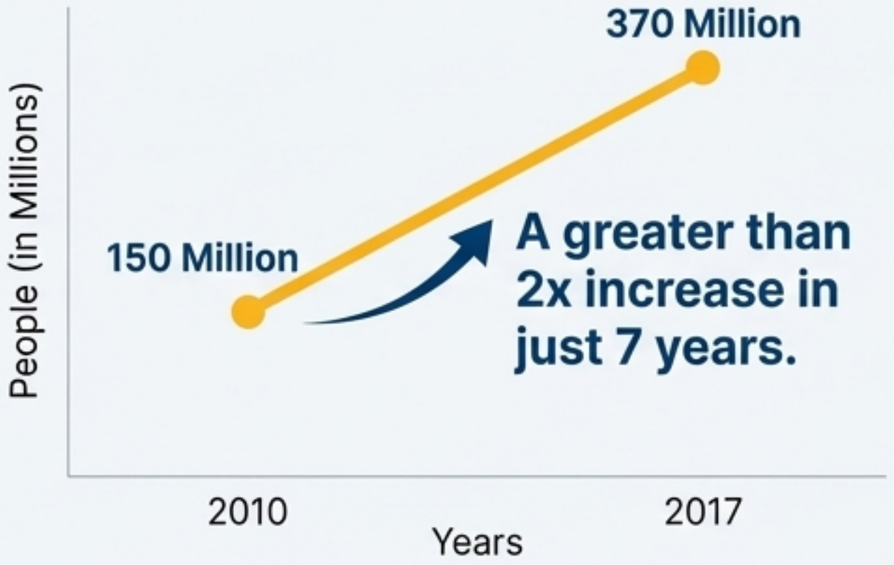
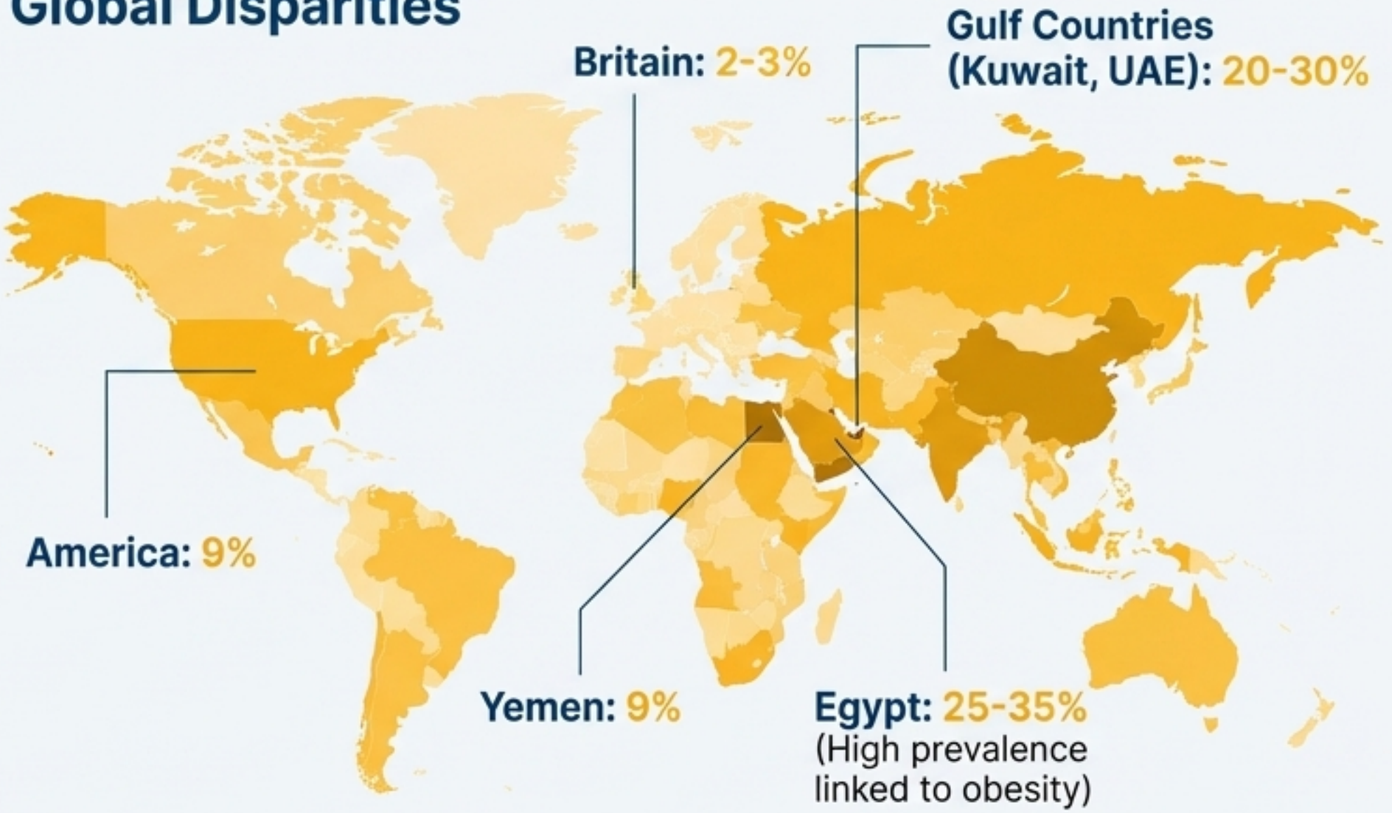
The Global Scale of the Diabetes Epidemic

Global Prevalence Growth



Global Disparities



The Hidden Burden

A significant number of individuals have "impaired diabetes" (prediabetes) and are undiagnosed, suggesting the true numbers are even higher.

Ethnic Disparities

Certain races, such as 'Nigros,' are noted to be more susceptible and develop diabetes earlier than Caucasians.

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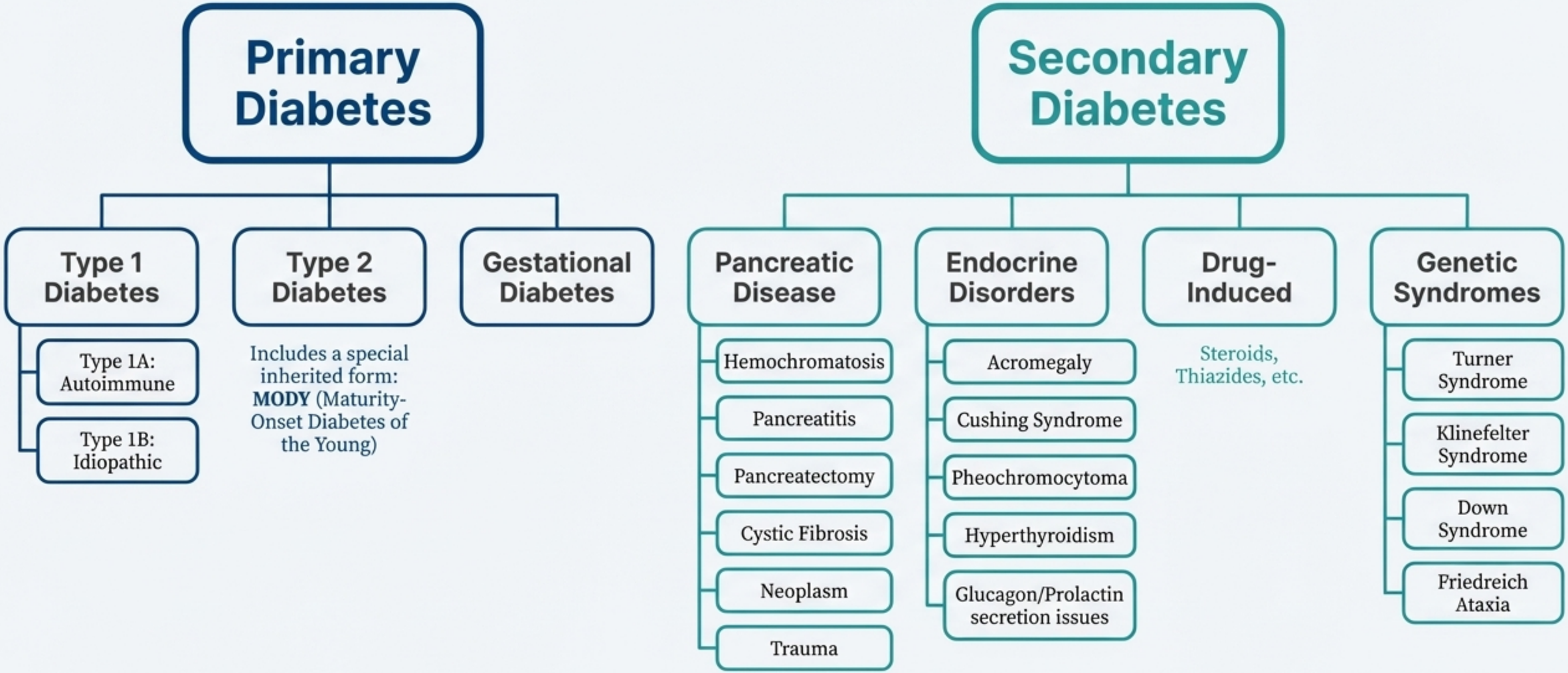
A Framework for Classification



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The Complex Web of Causality

The development of diabetes is multifactorial. Key contributing factors include:

Autoimmunity

The body's immune system attacks its own insulin-producing cells. This is the primary factor in Type 1.

Genetics

Critical in both types, but more pronounced in Type 2.

Concordance in identical twins: almost 100% for Type 2 vs. 30% for Type 1.

HLA-DQ3 and chromosome 6 variants are linked to Type 1.

Infections

Viral infections can trigger the autoimmune process in Type 1 (e.g., Coxsackie B, Mumps, Mengo virus).

Lifestyle

Sedentary lifestyles increase susceptibility.

Diet & Environment

Theories include the ‘depletion theory’ and early exposure to cow's milk. Poverty is a high-risk factor.

Age

Risk increases, especially after age 40.

Drugs

Steroids, Thiazides, Phenytoin, Antipsychotics, Fluoroquinolones, Pentamidine.

Pregnancy

Hormonal changes can induce gestational diabetes.

Radiation

A contributing environmental factor.

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Pathogenesis: A Tale of Two Types

Type 1 Diabetes: A Pathway of Destruction

Trigger: Autoimmune Process / Viral Infection

Action: Destruction of Pancreatic β-cells

Result: **Absolute Deficiency of Insulin**

Outcome: Overt Diabetes Mellitus

The main cause is autoimmune destruction.
Insulin levels are essentially zero.

Type 2 Diabetes: A Process of Resistance and Failure

Phase One: Initial Disturbance in Insulin Secretion (Defect or Delay)

Action: **Insulin Resistance** Develops in Peripheral Tissues

Result: ↑ Glucose, ↑ FFAs, ↑ TGs → “Sugar Toxicity”

Outcome: Overt Diabetes Mellitus (β-cell failure)

Key Concepts

- **Honeymoon Period**: Temporary remission after initial treatment.
- **Stunting Phenomenon**: Reversible β-cell dysfunction from prolonged hyperglycemia.

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The Physiological Cascade of Insulin Deficiency

Deficiency of Insulin

Carbohydrate Metabolism

↓ Glucose Uptake + ↓ Glycogenesis

Hyperglycemia

- Diuresis → **Polyuria → Polydipsia** & Fluid/Electrolyte Depletion
- **Polyphagia**

Fat Metabolism

Stimulation of Lipolysis

↑ Free Fatty Acids (FFAs)

Toxic in high concentrations.

Weight Loss

Protein Metabolism

Stimulation of Protein Degredation

↑ Amino Acids (AAs)

Weight Loss & Muscle Wasting

Underlying Vascular Theory

Increased LDL & Oxidants (Free Radicals) → Endothelial Cell Damage

Microangiopathy

Neuropathy
Retinopathy
Nephropathy

Macroangiopathy

Ischemic Stroke
MI
Diabetic Foot

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The Clinical Presentation of Diabetes

1. Classical Manifestations

- Polyuria, Polydipsia, Polyphagia
- Blurred vision, dry mouth
- Unexplained weight loss, muscle wasting
- Fatigue, insomnia
- Recurrent infections
- Nocturia

2. Incidental Finding

- Discovered during a routine examination (e.g., for employment or an annual check-up) in an asymptomatic patient.

3. Acute Complication

- The first presentation is a medical emergency:
  - Diabetic Ketoacidosis (DKA)
  - Diabetic Coma
  - Myocardial Infarction (MI) or Stroke
  - Severe Infection

4. Chronic Complication

- The patient presents with symptoms of long-term damage:
  - Retinopathy (vision problems)
  - Nephropathy (kidney problems)
  - Neuropathy (nerve pain/numbness)
  - Diabetic Foot ulcer

"Clinical Note: Patients may be in denial about chronic complications, attributing symptoms to other causes."

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Diagnostic Criteria: The Definitive Numbers

Key Diagnostic Notes

- **Fasting**: Defined as no caloric intake for at least 8 hours (overnight).
- **HbA1c**: Reflects average glucose over the past 2-3 months. Now used for diagnosis.
- **Urine Glucose**: Not used for diagnosis due to variable renal threshold.

Diagnostic Table (Non-Pregnant Adults)

	Normal	Impaired Glucose Tolerance (Prediabetes)	Diabetes Mellitus
Fasting (mg/dl)	<100	100 - 125	≥126
Random (mg/dl)	<140	140 - 199	≥200 + Clinical Features
HbA1c (%)	<5.7	5.7 - 6.4	≥6.5

Special Population: Pregnant Women

- Considered diabetic with a **Fasting glucose >92 mg/dl** or a **Random glucose >140 mg/dl.**
- **GTT Criteria: A single abnormal value is now required for diagnosis (e.g., Fasting >94 mg/dl).**

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The Philosophy of Management: Aims & Targets

Core Aims

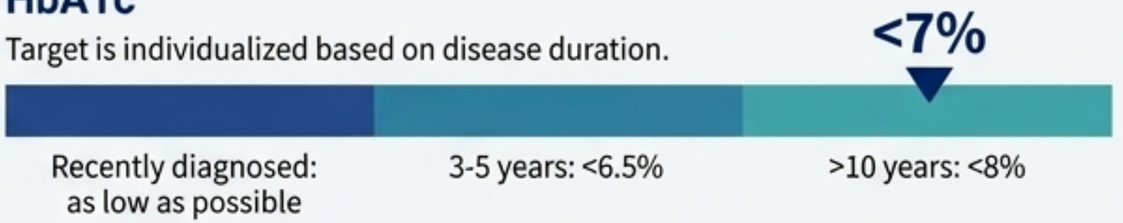
1. **A Life Free of Symptoms:** The primary and most important goal for the patient.
2. **Metabolic Control:** Glycemic (FBS, RBS, HbA1c) and Lipid (LDL) control.
3. **Maintain Ideal BMI:** Target range of 18-22.
4. **Control Blood Pressure.**
5. **Reduce Complications:** Good control leads to fewer complications.

Key Management Targets Dashboard

Blood Glucose (mg/dl)

HbA1c

Target is individualized based on disease duration.



LDL Cholesterol

Blood Pressure

<140/90 mmHg

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The Pillars of Care: Education, Diet, and Exercise

1. Patient Education

Ethical Obligation: Spend at least 10 minutes explaining the diagnosis.

Key Topics: Nature of the disease, complications, diet, exercise, therapy, insulin technique and storage.

Follow-Up: Regular visits (every 3-6 months) for exams, tests, and ophthalmology referral (every 6 months).

2. Diet

Non-Strict Diet (Preferred): Focuses on consistency. Best foods have a low glycemic index (e.g., grapefruit, barley).

Strict Diet: Reserved for specific cases (children, young, elderly) and depends on weight status to achieve ideal BMI.

3. Exercise & Activity

Benefits: Reduces blood sugar and lipids, defends blood vessels.

Aerobic: Swimming, brisk walking. Aim for 150 minutes/week (30 mins, 5x/week).

Non-aerobic: Wrestling, stretching.

Note: 90% of diabetic patients require aerobic exercise.

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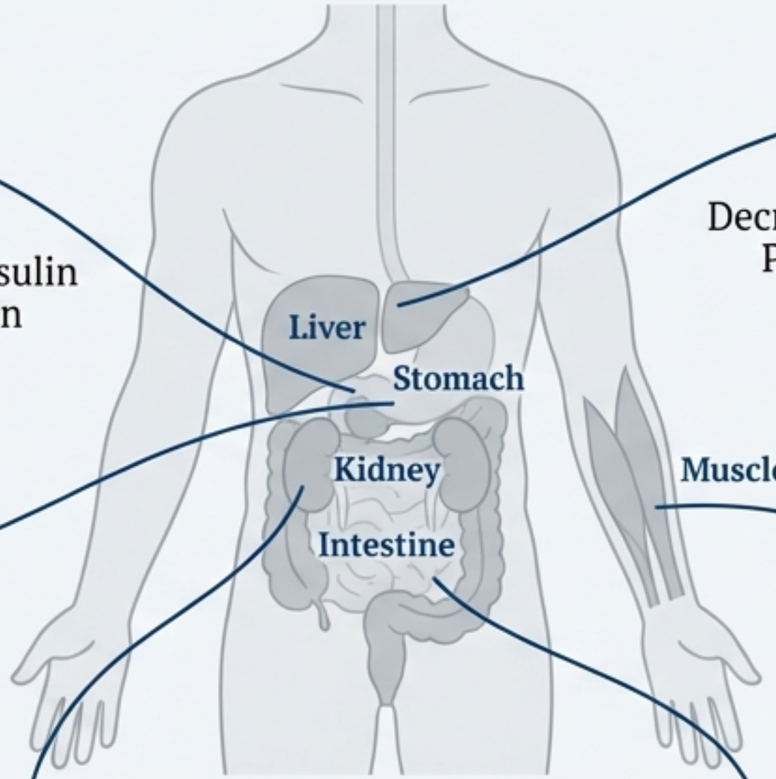
Oral Hypoglycemic Agents: A Strategic Overview



Sulfonylureas
Incretins (GLP-1, DPP-4i)
Repaglinide
Increase Insulin Secretion

Metformin
Decrease Glucose Production

Amylin
Delay Gastric Emptying

Metformin,
Pioglitazone
Increase Glucose Uptake

SGLT-2 Inhibitors
Increase Glucose Excretion

α-Glucosidase Inhibitors,
Metformin,
Incretin Group
Decrease Glucose Absorption

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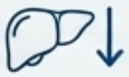
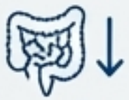
A Deeper Dive: Key Oral Medications

Biguanides (Metformin)

Mechanism of Action



1. Suppresses glucose production from the liver (main mechanism).



2. Decreases glucose absorption from the intestine.

3. Sensitizes peripheral tissues to insulin.

Key Advantages

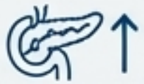
- ✓ Does not cause hypoglycemia.
- ✓ May cause slight weight reduction.
- ✓ Not carcinogenic.
- ★ Considered the best treatment, especially in early diabetes.

Side Effects

- ⚠ GIT upset, abdominal pain, flatulence, B12 deficiency.

Sulfonylureas (e.g., Glibenclamide, Gliclazide)

Mechanism of Action



Stimulates pancreatic β-cells to secrete insulin.

Generations

1st (obsolete), 2nd (Glibenclamide, Gliclazide, Glimepiride), 3rd.

Key Disadvantages / Side Effects

- ⚠ **Hypoglycemia** (significant risk).
- ⚠ **Weight gain**.
- ⚠ Depletion of the cells of the islets of Langerhans over time.

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Insulin Therapy: Key Indications

Insulin is the cornerstone of treatment in specific scenarios where oral agents are not sufficient or appropriate. The primary indications for initiating insulin therapy are:

1. **Type 1 Diabetes Mellitus:** Required for survival from the time of diagnosis.

2. **Gestational Diabetes:** When diet and exercise are not enough to control glucose levels.

3. **Failure of Oral Treatment:** In Type 2 DM, when maximum doses of oral agents fail to achieve glycemic targets.

4. **Periods of Acute Stress:** During major surgery, Myocardial Infarction (MI), or Sepsis.

5. **Diabetic Ketoacidosis (DKA):** An absolute requirement for treatment.

6. **Progressive, Unintentional Weight Loss:** A sign of severe insulin deficiency and catabolism.

7. **Patients with Complications:** Such as severe nephropathy or neuropathy where tight control with insulin is needed.

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Clinical Deep Dive: Managing Diabetic Ketoacidosis (DKA)

Case Vignette: A 45-year-old patient presents with distress, fatigue, polyuria, and dry mouth. On examination, they appear sick with shallow breathing and a BP of 70/100 mmHg.

1. Setting & Monitoring

- Immediate admission to ICU.
- Establish 2 IV lines, insert a urinary catheter.
- **Hourly monitoring**: Vital signs, Random Blood Sugar (RBS), electrolytes.

2. IV Fluid Rehydration (Top Priority)

- **Initial**: 0.9% Normal Saline (NS).
- **Initial**: 0.9% Normal Saline (NS). Give 1L in first 30 min, 500 mL in next hour, 1.5L over next 2 hours. (Total 3L in 3.5 hrs).
- **Transition**: When blood sugar reaches ~250 mg/dl, switch to 5% Dextrose (D5%) to prevent hypoglycemia and cerebral edema.

3. Insulin Therapy

- **Type**: Soluble (crystalline) insulin via IV infusion.
- **Dose**: Start with a loading dose (0.1 U/kg) followed by continuous infusion (0.1 U/kg/hr).
- **Goal**: Reduce blood sugar by ~54 mg/dl/hour. Continue until acidosis resolves.

⚠ Electrolyte Correction

- **Potassium (K+)**: CRITICAL
  - If K+ > 5.5 mEq/L: Do not give K+.
  - If K+ is 3.5-5.5: Correct K+ first, before starting insulin.
  - If K+ < 3.5: Give 40 mEq/L.
  - ***Never give K+ as a direct IV push.***
- **Bicarbonate**: Only consider if arterial pH < 7.0 due to risk of paradoxical CNS acidosis.

Criteria for Resolution

✅ Clinically well ✅ Normal BP ✅ No dehydration ✅ Normal electrolytes ✅ Negative ketones ✅ Patient can eat

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